(a) a nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO: 3;

(b) a nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence set forth in SEQ ID NO: 4; and,

(c) a nucleic acid molecule comprising an antisense nucleotide sequence of SEQ ID NO:3.

37. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:3, wherein said sequence encodes a polypeptide having LOX-like activity and said stringent conditions comprise hybridization in 50% formamide, 1 M NaCl, and 1% SDS at 37°C and a wash in 0.1x SSC at 60°C to 65°C.

42. (Amended) An isolated nucleic acid molecule comprising a nucleotide having at least 200 contiguous nucleotides of SEQ ID NO:3, wherein said sequence encodes a polypeptide having LOX-like activity.

REMARKS

Status of the Claims

Claims 2-4 and 25-46 were rejected. Claims 2, 27, 37,and 42 have been amended. Claims 2-4 and 25-46 are pending.

Amendments to the Claims

Claim 2 was amended to recite "90%" sequence identity. Support for this amendment can be found, for example, on page 15, lines 9-14 of the specification. Claim 2 was also amended to recite that the sequence identity to SEQ ID NO:3 is determined using the "GAP algorithm using default parameters". Support for this amendment can be found, for example, on page 25, lines 13-20.

Claim 37 was amended to correct a typographical error.

Claim 27 was amended to be independent.

Claim 42 was amended to recite "200 consecutive nucleotides". Support for this amendment can be found, for example, on page 14, line 15 of the specification.

No new matter has been entered by way of these amendments.

The Finality of the Rejection Should Be Withdrawn

The Office Action mailed January 15, 2003 was issued as a final action. Applicant respectfully submits that the finality of this action is improper and respectfully requests that finality be withdrawn.

As discussed in further detail in the Applicants rebuttal arguments related to the enablement rejection, the Office Action mailed January 15, 2003 asserts on page 5, paragraph 2, that claims (the specific claims encompassed are not specified in the action) are not enabled due to "codon bias". This assertion of lack of enablement was not made in the first Office Action mailed July 23, 2002 and was not necessitated by Applicants amendments. As the enablement rejection under 35 U.S.C. § 112, first paragraph, could have been made earlier and was not necessitated by the Applicant's amendments, the finality is improper. Therefore, Applicant respectfully submits that the finality of the office action be withdrawn.

In addition, the Office Action mailed January 15, 2003 asserts on page 5, paragraph 2, that claims (the specific claims encompassed are not specified in the Action) are not enabled since the claims recite "integration of the DNA of the invention into the genome of a cell, whereas the specification recites ligation of the DNA of the invention into an autonomous replicating expression vector". Again, this assertion of lack of enablement was not made in the first Office Action mailed July 23, 2002 and was not necessitated by Applicants amendments. As the enablement rejection under 35 U.S.C. § 112, first paragraph, could have been made earlier and was not necessitated by the Applicant's amendments, the finality is improper. Applicant respectfully submits that the finality of the office action be withdrawn.

The Rejection of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

Written Description

Claims 2-4, 25-26, and 37-46 remain rejected under 35 U.S.C. §112, first paragraph, for lack of sufficient written description. This rejection is respectfully traversed.

The Examiner maintains that the recitation of 80% sequence identity to SEQ ID NO:3, hybridization to SEQ ID NO:3, and a fragment comprising at least 50 contiguous nucleotides of SEQ ID NO:3 does not describe structural elements that are common among and unique to the claimed genus of nucleic acid molecules. While Applicants continue to maintain, the written description requirement has been satisfied as it relates to claims 2-4, 25-26 and 37-46, to expedite prosecution, the claims have been amended. Each amended claim as it relates to satisfying the written description requirements of 35 U.S.C. §112, first paragraph, are discussed below.

Claim 2 has been amended to recite that the sequence shares at least 90% sequence identity to the sequence of SEQ ID NO:3. The recitation of at least 90% sequence identity, as recited in claims 2-4 and 25-26, is a *very predictable structure* of the sequences encompassed by the claimed invention. Moreover, the claims recite the GAP algorithm to be used to determine the percent identity. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a sequence having at least 90% sequence identity to the sequence set forth in SEQ ID NO:3.

The description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common

to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). The recitation of a predictable structure of at least 90% sequence identity to SEQ ID NO:3 is sufficient to satisfy the written description requirement.

Moreover, an Applicant may rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id.*, *citing Lilly* at 1568. Claims 2-4 and 25-26 recite that the claimed sequences encode a polypeptide having LOX-like activity, thereby providing a functional characterization of the sequences claimed in the genus.

In the Amendment and Response filed on October 23, 2003, Applicants requested the Examiner to consider Example 14 of the Synopsis of Application of Written Description Guidelines. Again, Applicants submit that claims 2-4, 25 and 26 parallel this example. The Examiner is requested to reconsider the Example 14 in view of the amended claims that now recite at least 90% sequence identity to SEQ ID NO:3. As in Example 14, the specification discloses the nucleic acid sequence of SEQ ID NO:3, and the amended claims recite a limitation requiring the compound to have a specific function.

Consequently, contrary to the Examiner's conclusion, the sequences encompassed by the genus of claims 2-4 and 25-26 are defined by relevant identifying physical and chemical properties. In fact, the common attributes or features of the elements possessed by the members of the genus is that they encode a polypeptide having LOX-like activity and share at least 90% sequence identity at the nucleotide level to the disclosed nucleotide sequence of SEQ ID NO:3. The written description requirement of 35 U.S.C. §112, first paragraph, has been satisfied.

The Examiner further maintains the rejection of claims 42-46 for lack of written description which recite a sequence comprising at least 50 consecutive nucleotides of SEQ ID NO:1, wherein the sequence encodes a polypeptide having LOX-like activity. To expedite

prosecution claim 42 has been amended to recite a sequence comprising *at least 200 consecutive nucleotides* of SEQ ID NO:1.

The Examiner is respectfully requested to consider Example 15 of the Synopsis of Application of Written Description Guidelines in view of claims 42-46. Example 15 is drawn to antisense oligonucleotides of a novel sequence. Specifically, the claim at issue in the example is drawn to an antisense oligonucleotide complementary to SEQ ID NO:1, wherein said oligonucleotide inhibits the production of human growth hormone. While the claims at issue in the present invention are not drawn to antisense, Applicants submit the consideration for a sufficient description of a claimed genus as set forth in claims 42-46 of the instant invention and that set forth in Example 15 are the same.

Example 15 concludes sufficient written description exists as 1) SEQ ID NO:1 represents a member of the claimed genus, 2) the art would determine which oligonucleotides would have the recited activity, and 3) methods for making the oligos were routine in the art and accordingly the claimed invention was adequately described. In the instant case, claim 42-46 recite a nucleotide sequence having at least 200 consecutive nucleotides to SEQ ID NO:3 and the sequence encodes a polypeptide having LOX-like activity. Paralleling Example 15, the written description requirement has been satisfied: 1) SEQ ID NO:3 represents a member of the claimed genus; 2) the claims recite functional characteristics of the claimed invention and the specification provides assays to measure for LOX-like activity (page 15, lines 14-25); and 3) methods for generating 200 nucleotide fragments are routine in the art.

As exemplified by Example 15 of the Synopsis of Application of Written Description Guidelines, a genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). Accordingly, claims 42-46 satisfy the written description

requirement of 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdraw the rejection.

The Examiner further maintains the rejection of claims 37-41 which recite a nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:3. The claims further recite the specific conditions for the hybridization reaction. Applicants respectfully traverse.

Applicants disclose a single species encompassed by the claim (i.e., SEQ ID NO:3). A person of skill in the art would not expect substantial variation among the species encompassed by the scope of the claims because the highly stringent conditions set forth in the claims will yield structurally similar sequences. Moreover, the claims further provide a functional limitation that the claims encode a polypeptide having Lox-like activity. In view of the stringent hybridization conditions recited in the claims, the functional limitation that the sequence encodes a functional polypeptide recited in the claims, and the level of skill in the art, Applicants were clearly in possession of the claimed genus.

In summary, in view of the arguments above, claims 2-4, 25-26 and 37-46 satisfy the written description requirement of 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdraw the rejection.

Enablement

The rejection of claim 32 under 35 U.S.C. §112, first paragraph, was maintained for not satisfying the requirements of 37 CFR 1.808 related to the deposit of biological material. This rejection is respectfully traversed.

The Examiner states that the declaration filed on 7/23/02 is not sufficient to satisfy 37 CFR 1.808 as it does not state that 1) the deposit was made under the terms of the Budapest Treaty, and 2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent.

First, section 5, part c, of the declaration submitted on 7/23/02 clearly states "upon issuance of a patent, [applicant] irrevocably remove[s] all restrictions of access to the strain for the duration of the deposit". Accordingly, the statement requested by the Examiner is contained in the submitted declaration.

Second, 37 CFR 1.808 does not require a statement indicating the deposit was made under the terms of the Budapest Treaty. Instead, it sets forth requirements regarding the furnishing of samples. Applicants have chosen to *explicitly state each requirement* of the deposit under 37 CFR 1.808 instead of indicating that the deposit was made under the terms of the Budapest Treaty. Applicants submit that this is sufficient to satisfy the requirement. Part 5 a) and c) of the declaration submitted on 7/23/02 meet all of the requirements outlined in the cited rule. See also MPEP 2410.

In addition, the declaration filed on 7/23/02 further satisfies 37 CFR 1.806 regarding the terms of deposit. As stated in MPEP 2408 "unless applicant indicates that the deposit has been made under the Budapest Treaty, applicant must indicate the terms for which the deposit has been made." Section 5, part b2) and b3) of the declaration submitted on 7/23/02 expressly indicates all of the required terms outlined in 37 CFR 1.806.

In summary, an express statement of deposit under the terms of the Budapest Treaty is not required, *if the declaration explicitly makes the necessary statements under 37 CFR 1.806 and 1.808*. The Examiner is respectfully requested to withdraw the rejection of claim 32 under 35 U.S.C. §112, first paragraph, for lack of enablement.

Claims 2-4 and 24-46 remain rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. This rejection is respectfully traversed. Applicants note that the Office Action mailed January 15, 2003 acknowledges that the specification is enabling for a sequence of SEQ ID NO:3, a DNA construct comprising SEQ ID NO:3, and a transformed host cell comprising SEQ ID NO:3. Applicants agree with this statement. Claim 27 has been amended to become independent and recite a nucleic acid molecule set forth in SEQ ID NO:3, a nucleic acid molecule encoding the polypeptide of SEQ ID NO:4, or the antisense of SEQ ID NO:3. Accordingly, independent claim 27 and dependent claims 28-31 satisfy the enablement

requirements of 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdraw the rejection.

The Examiner continues to maintain that a sequence having 80% sequence identity to SEQ ID NO:1 is not enabled. While Applicants maintain claims drawn to 80% sequence identity are enabled, to expedite prosecution, claims 2-4 and 25-26 have been amended to recite a sequence having 90% sequence identity. Applicants submit that the amended claims 2-26 are fully enabled.

As made of record in the Amendment and Response filed on October 23, 2002, Applicants have provided the exemplary nucleotide sequences of SEQ ID NO: 3 and the exemplary polypeptide sequences of SEQ ID NO: 4. The sequences of the invention in claims 2-4 and 25-26 vary from these exemplary sequences by structural parameters (*i.e.*, percent sequence identity to SEQ ID NO: 3). Moreover, as amended, the claims now explicitly recite the GAP algorithm to be used to determine the percent identity. Further, the claimed sequences are required to retain LOX-like functionality. The specification provides guidance regarding methods for assaying the desired activity. See, for example, page 15, lines 14-25 that provides routine screening assays for LOX-like activity (i.e., LOX enzymatic activity or, alternatively, measuring an alteration in defense responses). Thus, one of skill in the art would readily be able to make a sequence encompassed by the claims and determine its functionality in a routine assay.

As Applicants stated in the previous response, the appropriate standard for determining whether undue experimentation would be required to make and use an invention is discussed in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and *In re Jackson*, 217 USPQ 804, 807 (Bd. Pat. App. & Int. 1982). *In re Wands* sets forth the "Wands factors," which are used by courts to assess whether experimentation is "undue." Thus, the applicability of *In re Wands* is not limited to experiments with antibodies but rather is relevant to a wide variety of molecular biology experiments. Applicants emphasize that it is now customary in the art to make a number of sequences and to test them in a large-scale assay for a desired function and that therefore, such experimentation is not "undue." For example, routine experiments involve what is commonly referred to as "shuffling," as described for example in U.S. Patent No. 5,837,458, issued November 17, 1998 with inventors Minshull and Stemmer and entitled, "Methods and

Compositions for Metabolic and Cellular Engineering." The art contains many examples of the use of such techniques. Thus, other publications such as Minshull and Stemmer ((1999) *Current Opinion in Chemical Biology* 3:284-290) and Christians *et al.* ((1999) *Nature Biotechnology* 17: 259-264) demonstrate that experiments comprising shuffling and large-scale functionality assays are now considered routine in the art. Because such experiments are routine, they would not be considered "undue experimentation" under *In re Wands* and *In re Jackson*. Accordingly, Applicants submit that the practice of the claimed methods does not require undue experimentation.

Applicants note that other cases involving molecular biology also support Applicants' position. *Hybritech Inc. v. Monoclonal Antibodies, Inc.* (231 USPQ 81 (Fed. Cir. 1986)) held that claims were enabled where the necessary method for producing monoclonal antibodies was well known in the art prior to the filing date. Similarly, in the recent case *Ajinomoto Co. v. Archer-Daniels-Midland Co.* (56 USPQ2d 1332 (Fed. Cir. 2000), *reh'g en banc denied* Nov. 14, 2000), the Federal Circuit found claims to be enabled where steps of the claimed method required the use of molecular biology techniques and a test for functionality. In finding that the claims were enabled, the court noted that "all of the methods needed to practice the invention were well known to those skilled in the art" and that "the process used conventional and well-known genetic engineering techniques." 56 USPQ2d at 1337.

The Office Action maintains that Broun *et al.* teaches the unpredictability in the field. Applicants continue to maintain, for the reasons made of record in the Amendment filed on October 23, 2003, that Broun *et al.* teaches away from making amino acid substitutions that conserve function of the polypeptide as claimed by the present invention. Moreover, Broun *et al.* used common techniques (similar to those outlined above) to identify the critical residues of the protein and subsequently change them to destroy the function of the polypeptide. The Broun *et al.* therefore provides further evidence that the techniques required to generate the sequences encompassed by the instant claims are routinely used in the art.

Accordingly, in view of the guidance in the specification and the knowledge in the art, claims 2-4 and 25-26 which recite 90% sequence identity to SEQ ID NO:3 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph.

Similarly, claims 42-46 have been amended to expedite prosecution and now recite a nucleic acid molecule having at least 200 consecutive nucleotides of SEQ ID NO:3, and encode a polypeptide having LOX-like activity. First, the state of the art is such that it would have been routine to make the DNA fragments encompassed by SEQ ID NO:3 given that SEQ ID NO:3 was provided in the specification. Moreover, as amended, the genus claimed is significantly smaller than a fragment of 50 consecutive nucleotides, and each embodiment can be readily identified in a manner routine in the art, synthesized using convention methods, and assayed for functional activity without using undue experimentation. Applicants, submit amended claims 42-46 are clearly enabled under 35 U.S.C. §112, first paragraph.

And finally, claims 37-41 recite a nucleotide sequence that hybridizes to the complement of SEQ ID NO:3 under the following conditions: hybridization in 50% formamide, 1 M NaCl, and 1% SDS at 37°C and a wash in 0.1x SSC at 60°C to 65°C. The Examiner asserts that adequate guidance is not provided to enable the claimed genus and indicates that an unspecified wash time in the claim leads to the lack of enablement. Applicants respectfully traverse.

Hybridization techniques are very well established in the art. One of skill would recognize that a wash would be maintained until equilibrium was reached. If one of skill desired the stringency of the wash conditions to be varied, the temperature or salt concentration would be altered. As evidence of this common understanding in the art, Applicant provide an excerpt from Moore and Dowhan, "Preparation and Analysis of DNA: Hybridization Analysis of DNA Blots," *Current Protocols in Molecular Biology*, 2002, Chapter 2.10.11, Supplement 26, John Wiley and Sons, New York. The excerpt concludes that the stringency of wash conditions are manipulated based on the Tm calculation and that the manipulation of stringency occurs via a change in temperature or salt concentration. This approach allows for the high level of reproducibility seen in the art as it relates to hybridization assays.

> *Designing washes for heterologous hybridization*. Calculations of T_m become more critical if heterologous probing is being attempted. If the aim is to identify sequences that are merely related, not identical, to the probe (e.g., members of a multigene family, or a similar gene in a second organism), then it is useful to have an idea of the degree of mismatching that will be tolerated by a "moderate-" or "low-" stringency wash. The best way to approach this is to first establish the lowest temperature at which only homologous hybridization occurs with a particular SSC concentration. Then assume that 1% mismatching results in a 1°C decrease in the T_m (Bonner *et al.*, 1973) and reduce the temperature of the final wash accordingly (for example, if sequences with ≥90% similarity with the probe are being sought, decrease the final wash temperature by 10°C). If the desired degree of mismatching results in a wash temperature of <45°C, then it is best to increase the SSC concentration so that a higher temperature can be used. Doubling the SSC concentration results in a ~17°C increase in T_m, so washes at 45°C in 0.1xSSC and 62°C in 0.2xSSC are roughly equivalent. Note that in these extreme cases it may also be necessary to reduce the hybridization temperature to as low as 45°C (aqueous solution) or 32°C (formamide solution).

One of skill would recognize that the length of the wash recited in claims 37-41 is carried out for at least the length of time it is required to establish equilibrium. Wash time extending beyond equilibrium will not influence the outcome. The claims at issue recite a specific temperature and salt concentration and thus clearly define the stringency of the wash conditions. Accordingly, the lack of a wash time recited in the claims does not render the claims non-enabled. Applicants maintain that all of the steps required to identify member of the claimed genus of claims 37-41 are known in the art.

In light of the discussion above, it is apparent that those of skill in the art would be able to practice the present claims without undue experimentation. Accordingly, the enablement rejection of claims 2-4, 25-26, and 37-36 should be withdrawn.

The Examiner asserts that a cell having stably introduced into its genome a nucleotide sequence of the invention is not enabled since "the use of animal and insect cells expression systems would be problematic" due to codon bias. First, the claims encompassed by this rejection were not specified. The Examiner is respectfully requested to clarify which claims

have been rejected. Second, the Examiner provides only a mere assertion of the difficulty of "condon bias". As noted in *In re Ahlert*, 165 USPQ 418, 420 (CCPA 1970) the notice of facts beyond the record which may be taken by the Examiner must be "capable of such instant and unquestionable demonstration as to defy dispute." The Examiner is respectfully requested to provide documentary evidence in the next Office Action if the rejection is maintained. Third, the assertion that claims drawn to cells are not enabled due to "codon bias" constitutes a new issue or new ground of rejection that was not necessitated by Applicants amendments. Accordingly, if the rejection is maintained, the Examiner is respectfully requested to withdraw the finality of the rejection.

The Examiner further states "Applicant claims integration of the DNA of the invention into the genome of a cell, whereas the specification recites ligation of the DNA of the invention into an autonomous replicating expression vector". The claims encompassed by this rejection have not be specified. If the rejection is maintained, the Examiner is respectfully requested to clarify.

Contrary to the assertion in the Office Action, the specification does not recite only "ligation of the DNA of the invention into an autonomously replicating vector". See page 36, line 14-19 of the specification that states "[i]t is expected that those skilled in the art are knowledgeable of in the numerous expression systems available for expression of a nucleic acid". Moreover, the specification discloses a variety of expression cassettes and DNA constructs. See page 38-45 of the specification. Accordingly, the specification dose not simply teach a DNA construction in an autonomously replicating vector.

In addition, the Applicants are unclear as to how this statement relates to the enablement of the instant claims. Absent an understanding of the claims that the rejection encompasses, the Examiner's assertion cannot be adequately addressed. However, if the Examiner intended the rejection to be applied to the claims of the instant invention that the recite a cell having "stably incorporated into the genome a nucleic acid molecule" of the invention, these claims recite that the sequence is *integrated into the genome*. These claims do not recite a limitation as to the transformation method used. Moreover, methods of transforming host cell are well known in the

art. As clearly explained throughout pages 38-45 of specification many techniques are commonly used. In addition, Example 3 and Example 4 of the specification provide commonly used methods for maize transformation, Example 5 provides commonly used methods for sunflower transformation, and Example 6 provides commonly used methods for soybean transformation. In view of the guidance provided in the specification and the skill in the art, one of skill would be able to generate a cell having the recited nucleotide sequence of interest integrated into its genome. Applicants submit that the claims of invention are enabled.

And finally, the Examiner's assertion regarding the lack of enablement as it related to the "autonomously replicating vector" again constitutes a new issue or new ground of rejection as it was not addressed in the first Office Action (mailed July 23, 2003) and it was not necessitated by Applicants amendments. Accordingly, if the rejection is maintained, the Examiner is respectfully requested to withdraw the finality of the rejection and to provide further clarification of the rejection.

The Rejection of the Claims Under 35 U.S.C. §102 Should Be Withdrawn

Claims 37-41 were rejected under 35 U.S.C. §102 as being anticipated by Rance *et al.* (1998) *PNAS* 95:6554-6559. The Examiner maintains that Rance *et al.* teaches a LOX gene that would hybridize to the complement of SEQ ID NO:3 under stringent conditions as recited in claims 37-41. This rejection is respectfully traversed.

As made of record in the Amendment and Response filed on October 23, 2003, the Examiner has provided nothing more than a mere assertion that the reference discloses sequences related to the claimed invention. The Amendment of October 23, 2003, requested if that if the rejection under 35 U.S.C. §102 in view of Rance *et al.* is maintained or applied to the newly submitted claims, the Examiner was respectfully requested to provide a Blast analysis which demonstrates the relationship of the claimed sequences to those disclosed by Rance *et al.* Such an alignment did not accompany the instant Office Action. Applicants respectfully continue to assert that the burden regarding the teaching of Rance *et al.* has not be established.

To expedite prosecution, Applicants have determined that the sequence used by Rance *et al.* corresponds to GenBank Acc. No. X84040. See page 6555, column 1, paragraph 7. A

Clustal W alignment revealed that GenBank Acc. No. X84040 shares 53% overall sequence identity to SEQ ID NO:3 and the longest region of consecutive sequence identity to SEQ ID NO:3 comprises 17 nucleotides. A sequence sharing this low level of sequence identity to SEQ ID NO:3 would not hybridize under the stringent hybridization conditions recited in claims 37-41.

The instant claims explicitly state that the hybridization conditions comprise hybridization in 50% formamide, 1 M NaCl, and 1% SDS at 37°C and a wash in 0.1x SSC at 60°C to 65°C. As evidence that a sequence having 53% overall sequence identity to SEQ ID NO:3 would not hybridize under these conditions, Applicants draws the Examiner's attention to page 22 of the specification and to Moore and Dowhan, "Preparation and Analysis of DNA: Hybridization Analysis of DNA Blots," *Current Protocols in Molecular Biology*, 2002, Chapter 2.9.8, Supplement 13, John Wiley and Sons, New York, both of which set forth the following commonly used equation to determine hybridization conditions:

$$Tm = 81 + 16.6\log 10Ci + 0.4[\%(G+C)] - 0.6(\%\ \text{formamide}) - 600/n - 1.5(\%\text{mismatch})$$

where
Ci = molar concentration of monovalent cations
n = length of the annealed product

In view of this equation, convenient hybridization temperatures in the presence of 50% formamide are 42°C for a probe which is 95-100% homologous to the target fragment, 37°C for 90-95% homology, and 32°C for 85 to 90% homology. Since the claims of the instant invention recite hybridization occurring in 50% formamide at 37°C, any target sequence having less than 90% homology to SEQ ID NO:3 will not hybridize to the sequence of SEQ ID NO:3. Accordingly, claims 37-41 are novel in view of Rance *et al.*

And finally, the Office Action implies that the claims require the recitation of the length of the wash conditions to distinguish over the cited art. As discussed above, one of skill will recognize that the wash time will be carried out for a time period sufficient to establish equilibrium. The limitation is not required to overcome the novelty rejection.

Accordingly, Applicants submit that claims 37-41 are not anticipated by Rance *et al.* and the Examiner is respectfully requested to withdraw the rejection.

Consideration Of Previously Submitted Information Disclosure Statement

It is noted that an initialed copy citation #31 appearing on the PTO Form 1449 that was submitted with Applicants' Information Disclosure Statement filed April 25, 2001 has not been returned to Applicants' representative with the Office Action. Accordingly, it is requested that citation #31 be initial and the initialed copy of the Form 1449 be forwarded to the undersigned with the next communication from the PTO. Copies of the cited references were provided at the time of filling the original Information Disclosure Statement, and, therefore, no additional copies of the references are submitted herewith. Applicants will be pleased to provide additional copies of the references upon the Examiner's request if it proves difficult to locate the original references.

CONCLUSIONS

The Examiner is respectfully requested to withdraw the rejections and allow claims 2-4 and 25-46. In any event, the Examiner is respectfully requested to enter the above amendments for purposes of further prosecution. The amendments were made pursuant to suggestions made by the Examiner. It is believed that all of the outstanding rejections have been addressed and the claims are ready for allowance. Early notice to this effect is solicited.

Should the Examiner have further questions or comments with respect to examination of this case, it is respectfully requested that the Examiner telephone the undersigned so that further examination of this application can be expedited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those, which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required

therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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CERTIFICATION OF FACSIMILE TRANSMISSION	CERTIFICATE OF MAILING
I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office at Fax No. 703-872-9307on the date shown below. Pamela Lockley (Type or print name of person signing certification.) Signature — March 17, 2003 Date	I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: **BOX AF**, Commissioner for Patents, Washington, DC 20231, on March 17, 2003. _____

Version with Markings to Show Changes Made:

2. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence having at least [80%] 90% sequence identity to the sequence set forth in SEQ ID NO: 3, wherein said sequence encodes a polypeptide having LOX-like activity and wherein said sequence identity to SEQ ID NO:3 is determined using the GAP algorithm using default parameters.

27. (Amended) [The isolated nucleic acid molecule of claim 2, wherein said] An isolated nucleic acid molecule comprising a nucleotide sequence [is] selected from the group consisting of:

(a) a nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO: 3;

(d) a nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence set forth in SEQ ID NO: 4; and,

(e) a nucleic acid molecule comprising an antisense nucleotide sequence of SEQ ID NO:3.

37. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:3, wherein said sequence encodes a polypeptide having LOX-like activity and said stringent conditions comprise hybridization in 50% formamide, 1 M NaCl, and 1% SDS at 37°C and a wash in 0.1x SSC at 60°C to 65°C.

42. (Amended) An isolated nucleic acid molecule comprising a nucleotide having at least [50] 200 contiguous nucleotides of SEQ ID NO:3, wherein said sequence encodes a polypeptide having LOX-like activity.